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Paper Trail: Working Paper and Recent Scholarship

Editors' Note: *This edition reviews a paper by Castanheira et al. that describes theoretical and empirical research which attempts to model and measure the effects of a situation that the authors refer to as an "asymmetric competition shock" by looking to pharmaceutical markets and the effects of generic product launches in those markets.*

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—*William H. Page and John R. Woodbury*

Recent Papers

Micael Castanheira, Carmine Ornaghi, Georges Siotis & Marie-Angeles de Frutos,
The Unexpected Consequences of Asymmetric Competition. An Application to Big Pharma
(Center for Economic Policy Research Discussion Paper DP11813, Jan. 27, 2017),
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2908226

This paper by Micael Castanheira, Carmine Ornaghi, Georges Siotis, and Marie-Angeles de Frutos describes theoretical and empirical research that attempts to model and measure the effects of a situation that the authors refer to as an "asymmetric competition shock." In this context, the authors consider an asymmetric competition shock to be an event that differentially affects existing competitors.

To help motivate and empirically test a theoretical model of an asymmetric competition shock that the authors develop, they look to pharmaceutical markets and the effects of generic product launches in those markets. In recent years, many antitrust cases have been brought for which the alleged competitive harm stems from alleged delay or foreclosure of the launch of generic versions of a branded pharmaceutical product. At the heart of these cases are several different mechanisms through which generics are alleged to have been delayed or foreclosed. Mechanisms that are accused of having this effect include so-called reverse payment patent settlements that are alleged to be engineered to delay generic entry and the development of new drug formulations that are alleged to frustrate the launch of generic products by inhibiting their ability to take advantage of institutional structures that facilitate their being dispensed by pharmacies. Accordingly, this research may be of interest to antitrust practitioners.

The authors describe pharmaceutical markets as being "oligopolistic and differentiated" with advertising and promotion used as key competitive strategies by some market participants.[1] As such, they recognize the substitutability of products that are used to treat the same medical condition.[2]

[1] Micael Castanheira, Carmine Ornaghi, Georges Siotis & Marie-Angeles de Frutos, *The Unexpected Consequences of Asymmetric Competition. An Application to Big Pharma* 3 (Center for Economic Policy Research Discussion Paper DP11813, Jan. 27, 2017).

[2] *Id.* at 3.

The authors also recognize that generic versions of branded drugs are typically launched at the time that the branded versions lose patent protection.[3] They consider the first entry of a generic version of a branded drug to be an asymmetric competition shock because it can differentially affect the products within a particular therapeutic class of drugs. In this context, a therapeutic class of drugs generally means a set of products that are used to treat the same medical condition. The authors observe that, following the launch of the first generic versions of a drug, typically (1) a substantial portion of the sales that, but for the launch of the generic versions, would have gone to the branded version are converted to the generic versions and (2) the advertising and promotional efforts for the branded version are stopped.

Under these circumstances, the authors have observed that, although the prices of generic drugs tend to be lower than their branded reference products (and often by a substantial margin), there are cases for which, following the launch of low-priced generic products, the total branded plus generic unit sales of the product decline, while the sales of other products within the same therapeutic class increase. The authors attribute this effect to changes in the relative promotional efforts for the products—in particular, because the branded products without generic versions continue to engage in promotion, the demand-building effects of those efforts dominate the low price of the new generic entrants.[4] Based on that result, they conclude "that generics display two different faces: while they are fierce competitors for the branded drug that lost exclusivity, they appear to be toothless challengers with respect to the remaining patent-protected drugs."[5]

Theoretical Model

To formalize these anecdotal observations, the authors build a simple model of a market with two different products (A and B) that experiences entry of a new product that is a perfect substitute for one of the incumbent products.[6] In their model, (1) firms compete through price and non-price (specifically, persuasive advertising) instruments; (2) purchasing behavior is made through an intermediary who can be persuaded; (3) one of the incumbent products (A) faces the entry of a new product that is assumed to be a perfect substitute (G).

The authors suggest that competition between A and G implies that the price of A will drop and, because G can "free-ride" off of the advertising efforts of A, the level of promotion for A will also fall. However, the authors indicate that the effect of the entry of G on B's sales is ambiguous: the lower price of A may have a negative effect on B's sales, but the reduced promotional efforts by A may have a positive effect. The model that the authors construct suggests how various factors, such as patient price sensitivity and the degree of horizontal differentiation between A and B, may affect the post-entry change in the market share of B.

The model assumes (1) that a patient/physician pair (PPP) gains an "intrinsic utility" from using each product that can be affected by the level of advertising and the PPP's sensitivity to price and (2) the PPPs are heterogeneous. PPPs choose the product that maximizes their utility, which yields the demand curve for each product. Manufacturers are allowed to choose the prices of their products, as well as a level of promotional activity. Promotional activity is modeled as a cost that increases demand for the product by increasing its utility.

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[3] *Id.*

[4] *Id.* at 1–3.

[5] *Id.* at 8.

[6] *Id.* at 10–17.

In the end, the model predicts that when G enters, all else equal, B should realize larger gains in market share (1) the less price sensitivity among the PPPs; (2) the less differentiation between A and B; and (3) the larger the overall market defined by A and B. Based on these findings, the authors conclude:

> It is striking that it is precisely when A and B are closer substitutes . . . that stiffer price competition by the generic versions of A allows B to increase its market share. Conversely, only if the two molecules are sufficiently distant substitutes or if market size . . . is small, will price competition have the (*a priori* expected) effect of boosting the sales of molecule A.[7]

Empirical Analyses

To test these predictions, the authors perform several regression analyses using data on historical pharmaceutical sales and promotional efforts.[8] Specifically, for these analyses they use quarterly data from IMS Health on dollar sales revenues and quantities sold for hundreds of branded and generic prescription drugs sold in the United States from 1994 through 2003. As discussed below, from these data they are able to observe sales in two separate channels: hospitals and pharmacies.[9] The authors also use data from IMS Health that report expenditures on efforts to promote drugs to doctors, including for physician detailing, providing free samples to physicians to give to their patients, and advertising in professional journals.

First, the authors analyze pharmaceutical demand without the effects of within-molecule generic entry.[10] To that end, they look at drug prices, quantities, and promotion during the time periods *before* a drug loses exclusivity (i.e., generic versions are launched and sold). The authors make several empirical observations based on this analysis: (1) elasticity of demand with respect to prices is higher for hospitals than for pharmacies; (2) promotional efforts affect a drug's own sales positively and competitors' sales negatively; and (3) generic entry does not have a meaningful effect on branded sales. To obtain these results, the authors use a regression analysis that attempts to assess the relationship between a drug's market share (where the market is as defined by ATC3[11] therapeutic categories) and the drug's own price, the prices of competing drugs, measures of promotional efforts for the drug, and measures of promotional efforts for competing drugs, along with controls for the time remaining until patent expiration and likely entry of generic versions of the drug. This regression was performed separately for the hospital and pharmacy channels.[12]

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[7] *Id.* at 16.

[8] *Id.* at 18–21.

[9] The authors do not explain whether they are measuring sales (and prices) into these channels or the sales being dispensed out of these channels.

[10] *Id.* at 23–30.

[11] ATC is an acronym for Anatomical Therapeutic Chemical. The ATC system is a classification system for drugs. The authors state that "[t]he 'ATC3 level' corresponds to a market: it groups the drugs that target a given condition." Id. at 20. They also indicate that "the ATC3 class is associated with a pathology, while each of the ATC4 therapeutic sub-groups within the same ATC3 corresponds to different modes of action to treat that pathology." *Id.* at 33.

[12] To attempt to address endogeneity and measurement error in the price and promotion variables, which will cause the regression coefficients to be biased, the authors use an instrumental variables approach with the following instruments: the number of packages; the number of packages squared; the average price of drugs sold by the manufacturer in other ATC3 markets (for hospitals) and price of drug sold in hospitals (for pharmacy); and an indicator variable for a successful Paragraph IV challenge. They provide very little intuition as to why these are valid instruments.

As previously mentioned, the authors find that the own-price elasticity of demand (measuring the change in the quantity demanded of a product in response to a change in its price) at hospitals is higher than at pharmacies.[13] They attribute this result to circumstances that may make "consumers" of pharmacy-dispensed drugs less price sensitive compared to hospitals. Specifically, they cite the agency problem caused by physicians not having the direct financial incentive to account for drug prices in their prescribing decisions, as well as the fact that patients generally tend not to bear the entire cost of a prescription drug because of insurance benefits.

Additional inquiry would be useful to test if these results are robust. For example, the data used by the authors to measure drug prices do not account for rebates that are paid by drug manufacturers as a result of contracts that they enter with managed care organizations. Because of the strategic and competitively significant nature of these rebates, they are typically confidential and thus difficult for researchers to obtain. That said, it would be interesting to consider and, if possible, test how the results of these analyses are sensitive to the price constraints imposed by managed care contracting.

In this analysis, the authors also find that cross-price elasticities (measuring the change in the quantity demanded of a product in response to a change in the price of another product) are very small in magnitude and not statistically distinguishable from zero between the branded drugs in this analysis and competing generic drugs (which are not therapeutically equivalent but in the same therapeutic class), but are much larger (especially for hospital buyers) between the branded drugs analyzed and competing branded drugs.

In their second set of empirical analyses, the authors look at the effect on generic drugs of the loss of brand exclusivity by regressing generic market shares following the loss of brand exclusivity on the prices of other generic products (with the same and different branded reference products), the branded version's price, the prices of other branded competitors, as well as the measures of promotional efforts describe above.[14] From this regression, the authors estimate large own-price elasticities for generics and significant positive cross-price elasticities between other generic versions of the same drug. They also find little influence of other competing drugs' (brand or generic) prices on generic share, but some negative effect by competing brands' promotional efforts.

The authors conclude that their results from these two analyses suggest that "competition is *inter*-molecular while drugs are on patent" and it "shifts to chiefly *intra*-molecular after" loss of exclusivity.[15]

Finally, the authors perform empirical tests of some of the implications of their theoretical model.[16] As discussed above, the model predicts that the "negative cross-price" elasticity effect should be amplified (i.e., competitors to the drug going off-patent for which generic versions are launched should gain more share) when (1) the price elasticity is smaller in magnitude; (2) the products in the market exhibit less differentiation; and (3) when the market is larger. They find empirical results that are consistent with these predictions. Specifically, they find empirical models that show the "negative cross-price" elasticity effect and that the effect is diminished in the

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[13] Again, as noted above, it is not clear if the data used by the authors is measuring drug purchases by these entities or drug dispensing in which they engage.

[14] *Id.* at 30–33.

[15] *Id.* at 33.

[16] *Id.* at 35–39.

hospital channel (which they found to be more price sensitive), diminished with each additional mode of action defined by the ATC4 classification (which they conclude is a proxy for more product differentiation), and diminished in smaller markets.

Conclusion

In sum, this paper raises some interesting theoretical and empirical observations about how pharmaceutical markets may respond to generic drug entry. Of particular note, the authors' findings implicate output effects from the launch of lower-priced generics and competition among therapeutic alternatives. As with any analysis of pharmaceutical markets, this analysis must contend with idiosyncratic features of those markets, including institutional structures that affect dispensing decisions and multiple layers of pricing and decision-making that affect prescribing and purchasing decisions. Among other issues, these features make measuring prices and price changes problematic.[17] The authors recognize some of these hurdles and attempt to address them with certain econometric techniques. To what extent those efforts are successful deserves further research and analysis. ●

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[17] These features include, e.g., the effects of managed care practices, such as manufacturer rebates and patient pharmacy benefit copays, which can promote competitive outcomes.